UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,933	02/27/2002	Peter Sondermann	HUBR-1189(10	7771

24972 7590 08/25/2004

FULBRIGHT & JAWORSKI, LLP
666 FIFTH AVE
NEW YORK, NY 10103-3198

EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 08/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,933	SONDERMANN ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *81-94* is/are pending in the application.

4a) Of the above claim(s) *87 –90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *81-86 and 91-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 05/10/04 is acknowledged.

Claims 81-94 are pending.

2. Applicant's election with traverse of Group III, claims 41-45, 59-61 and 77-78, now claims 81-86 and 91-94 as it reads on recombinant soluble FcγRIIb receptor and pharmaceutical composition, wherein said receptor contains SEQ ID NO:3 in the reply filed on 05/10/04 is acknowledged. Applicant traverse the Restriction Requirement on the grounds that Groups I-XXVII do relate to a single general inventive concept and do not lack unity and that examination all groups together would not constitute a serious search burden on the examiner.

This is not found persuasive because: (i) as was stated in the previous Office Action, the inventions listed as Groups I-XXVII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features over the prior art of record; (ii) the MPEP 803 (August 2001) states that "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search". The Restriction Requirement enunciated in the previous Office Action meets this criteria and therefore establishes that serious burden is placed on the examiner by the examination of more than one Group.

The requirement is still deemed proper and is therefore made FINAL.

Claims 87 –90 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 81-86 and 91-94 reads on recombinant soluble FcγRIIb receptor and pharmaceutical composition, wherein said receptor contains SEQ ID NO:3 under consideration in the instant application.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 81-86 and 91-94 are rejected under 35 U.S.C. 112, first paragraph are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

Applicant discloses a homogenous preparation of recombinant soluble FcγRIIb receptor, wherein said receptor contains amino acid sequence of SEQ ID NO: 3 that was used for crystallization and structure determination (see examples 1-3 in particular). The specification does not adequately teach a homogenous preparation of *any* recombinant soluble FcγRIIb receptor, as claimed in claim 81 or 83 or pharmaceutical composition, comprising *any* recombinant soluble FcγRIIb receptor, as claimed in claim 84 or pharmaceutical composition comprising recombinant soluble FcγRIIb receptor, wherein said receptor contains amino acid sequence of SEQ ID NO:3, as claimed in claim 92 to effectively treat autoimmune diseases, allergies or tumor diseases including AIDS, rheumatoid arthritis or multiple myeloma. Moreover, no animals models were used to study the effectively of treatment autoimmune diseases, allergies or tumor diseases, including AIDS, rheumatoid arthritis or multiple myeloma using disclosed homogenous preparation of any recombinant soluble FcγRIIb receptor or recombinant soluble FcγRIIb receptor wherein said receptor contains amino acid sequence of SEQ ID NO:3 . Thus it is unclear whether or not the claimed preparation and composition would function as pharmaceutical composition. In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the preparation and

pharmaceutical composition as claimed, and absence of working examples providing evidence which is reasonably predictive that the claimed preparation and pharmaceutical composition are effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition with a reasonable expectation of success. Feldman et al (Transplant. Proc. 1998, 30, 4126-4127) teach that "while it is not difficult to study the pathogenesis of animal models of disease, there are multiple constraints on analyses of the pathogenesis of human disease, leading to interesting dilemmas such as how much can we rely on and extrapolate from animal models in disease". In addition, Cochlovius et al (Modern Drug Discovery, 2003, pages 33-38) teach that in contrast to in vitro models, and partly animal-human xenograft systems, tissue cells in vivo seems to express molecules for defense against cellular immune systems as well as against complement. Although these defense mechanisms are still poorly understood, they provide some hints as to why many potential therapeutics perform marvelously in vitro but a fairly high portion of them still fail in vivo. Feldman et al . further teach that in a chronic immune-driven inflammatory response there are a number of pathways that become engaged and effective therapy in immune inflammatory diseases such as rheumatoid arthritis, will come from therapy aimed at several points in the disease pathway. Moreover, Aoki et al (US Patent 5,470,578) teach that the cause of a chronic multiple inflammatory disease, rheumatoid arthritis, is still unknown and no reliable treatment of the disease has been established (see entire document, column 1, lines 55-60 in particular).

Also an issue that Applicant has not taught how to make a homogenous preparation of *any* recombinant soluble receptor FcγRIIb , other than homogenous preparation of recombinant soluble FcγRIIb receptor, wherein said receptor contains amino acid sequence of SEQ ID NO: 3. The structural and functional characteristics of said *any* recombinant soluble receptor FcγRIIb are not defined in the claim.

Applicant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated *any* recombinant soluble receptor FcγRIIb encompassed by the claimed invention other than homogenous preparation of recombinant soluble FcγRIIb receptor, wherein said receptor contains amino acid sequence of SEQ ID NO: 3 would be expected to have greater differences in their activities.

Protein chemistry is probably one of the most unpredictable areas of biotechnology . It is known in the art that even single amino acid changes or differences in a proteins amino acid sequence can have dramatic effects on the protein's function. For example, Mikayama et al. (PNAS, 1993. 90: 10056-10060) teach that the human glycosylation factor (GIF) protein differs from human macrophage migration inhibitory factor (MIF) by a single amino acid residue (see Figure 1 in particular). Yet, Mikayama et al. further teach that GIF is unable to carry out the function of MIF and MIF does not demonstrate GIF activity (see Abstract in particular). Burgess et al (J Cell Biol. 111:2129-2138, 1990) show that a conservative replacement of a single "lysine" reside

at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Similarly, Lazar et al. (Mol Cell Biol. 8:1247-1252, 1988) teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagines did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Furthermore, the specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed sequence can be tolerated that will allow any recombinant soluble FcγRIIb receptor to function as claimed. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited.

Since the instant fact pattern fails to indicate that representative number of structurally related compounds is disclosed, the artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claims and consequently would not know how to make them. An assay for *finding* a product is not equivalent to a positive recitation of *how to make* a product.

Also the isuues is that the burden of enabling the prevention of a disease (i. e. the need for additional testing) would be greater than that of enabling a treatment due to the need to screen those humans susceptible to such diseases and the difficulty of proof that the administration of the drug was the agent that acted to prevent the condition. Further, the specification does not provide guidance as to how one skilled in the art would go about screening those patients susceptible to autoimmune diseases, allergies or tumor diseases, including HIV infection and AIDS within the scope of the presently claimed invention. Nor is guidance provided as to a specific protocol to be utilized in order to prove the efficacy of the presently claimed compounds in preventing these disease states. Accordingly, undue experimentation is necessary to determine screening and testing protocols to demonstrate the efficacy of the presently claimed invention.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed a homogenous preparation of *any* recombinant soluble receptor, as claimed in claim 81 or 83 or pharmaceutical composition, comprising *any* recombinant soluble FcγRIIb receptor, as claimed in claim 84 or pharmaceutical composition comprising recombinant soluble FcγRIIb receptor, wherein said receptor contains amino acid sequence of SEQ ID NO:3, as claimed in claim 92 to effectively treat autoimmune diseases, allergies or tumor diseases including AIDS, rheumatoid arthritis or multiple myeloma in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

6. Claims 81, 83, 84, 85, 86, 93 and 94 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : a homogenous preparation of recombinant soluble FcγRIIb receptor, wherein said receptor contains amino acid sequence of SEQ ID NO: 3.

Applicant is not in possession of : a homogenous preparation of *any* recombinant soluble FcγRIIb receptor, or pharmaceutical composition, comprising *any* recombinant soluble FcγRIIb receptor,

The claimed invention is drawn to a genus of recombinant soluble FcγRIIb receptor, however, structural identifying characteristics of the genus are not disclosed. There is no evidence that there is any *per se* structure/function relationship between the disclosed soluble FcγRIIb receptor, wherein said receptor contains amino acid sequence of SEQ ID NO: 3 and any others ; in essence, the specification simply directs those skilled in the art to go figure out for themselves what the claimed recombinant soluble FcγRIIb receptor looks like.

Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of a genus of claimed recombinant soluble FcγRIIb receptor may be achieved by means of a recitation of a representative number of polypeptide sequences, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry,

whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 37(c) of this title before the invention thereof by the applicant for patent.

8. Claims 81, 83 - 86, 93 and 94 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 5,623,053 as is evidenced by the known fact disclosed in the Specification on overlapping pages 4-5.

US Patent '053 teaches a pharmaceutical composition, comprising a recombinant soluble human Fcγ RII b receptor characterized by the absence of a transmembrane and signal peptide domain (see entire document, Abstract and columns 5 and 10 in particular). US Patent '053 teaches that the usefulness of the membrane-bound FcRn is limited and it might be beneficial to remove transmembrane domain from the FcRn to obtained soluble FcRn (see overlapping columns 4 and 5 in particular). US Patent '053 teaches that recombinant soluble receptor is obtained by expression of a nucleic acid in prokaryotes.(see Abstract and column 8 in particular). Though US Patent '053 does not explicitly teaches that expression of a recombinant soluble human Fcγ RII b receptor is performed under conditions that lead to production of insoluble inclusion bodies it is noted that the instant claims are drawn to a product (recombinant soluble FcγRIIb) and the patentability of the product does not depend on its method of production in the absence of evidence of structural difference. In re Thrope,227 USPQ 964,966 (Fed. Cir. 1985). See MPEP 2113.

As is evidenced in the specification on overlapping pages 4-5, at the time the invention was made one skill in the art was aware of the advantages of the expression of protein in prokaryotic cells, the production of the inclusion bodies and that the product that is expressed in prokaryotic cells is not glycosylated.

Claims 85, 86 , 93 and 94 are included because a composition is a composition irrespective of its intended use in the absence of evidence of structural difference.

The reference teaching anticipates the claimed invention.

9. Claims 81, 83-86 and 93-94 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,675,105 as is evidenced by the known fact disclosed in the Specification on overlapping pages 4-5.

US Patent '105 teaches a pharmaceutical composition, comprising a recombinant soluble human Fcγ RII b receptor of SEQ ID NO: 6 characterized by the absence of a transmembrane and signal peptide domain (see entire document, Abstract and columns 3, 5 and 14 in particular). It is noted that the referenced SEQ ID: 6 is 100 % identical to the claimed SEQ ID NO: 3 (see attached sequence alignment). US Patent '105 teaches that said pharmaceutical composition can be used for treatment of autoimmune diseases, allergies or tumor diseases (see columns 6 and 26 in particular). US Patent '105 teaches that recombinant soluble receptor is obtained by expression of a nucleic acid encoding said receptor in prokaryotes.(see overlapping columns 23-24 in particular). Though US Patent '105 does not explicitly teaches that expression of a recombinant soluble human Fcγ RII b receptor is performed under conditions that lead to production of insoluble inclusion bodies it is noted that the instant claims are drawn to a product (recombinant soluble FcγRIIb) and the patentability of the product does not depend on its method of production in the absence of evidence of structural difference. In re Thrope,227 USPQ 964,966 (Fed. Cir. 1985). See MPEP 2113.

As is evidenced in the specification on overlapping pages 4-5, at the time the invention was made one skill in the art was aware of the advantages of the expression of protein in prokaryotic cells, the production of the inclusion bodies and that the product that is expressed in prokaryotic cells is not glycosylated.

Claims 85, 86 , 93 and 94 are included because a composition is a composition irrespective of its intended use in the absence of evidence of structural difference.

The reference teaching anticipates the claimed invention.

10. No claim is allowed.

11. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
August 23, 2004

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600